

**THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Appellants: Bortlik, et al.
Appl. No.: 10/568,704
Conf. No.: 4852
Filed: February 16, 2006
Title: NATURAL LYCOPENE CONCENTRATE AND METHOD FOR
PRODUCTION THEREOF
Art Unit: 1655
Examiner: Qiuwen Mi
Docket No.: 3712036-00706

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANTS' APPEAL BRIEF

Sir:

Appellants submit this Appeal Brief in support of the Notice of Appeal filed on August 6, 2010. This Appeal is taken from the Final Rejection dated May 27, 2010.

I. REAL PARTY IN INTEREST

The real party in interest for the above-identified patent application on Appeal is Nestec S.A. by virtue of an Assignment dated May 10, 2006 and recorded at reel 017608, frame 0057 in the United States Patent and Trademark Office.

II. RELATED APPEALS AND INTERFERENCES

Appellants' legal representative and the Assignee of the above-identified patent application do not know of any prior or pending appeals, interferences or judicial proceedings which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision with respect to the above-identified Appeal.

III. STATUS OF CLAIMS

Claims 1, 3-12, 14 and 15 are pending in the above-identified patent application. Claims 6-8, 12, 14 and 15 were previously withdrawn from consideration, and Claims 2 and 13 were previously canceled without prejudice or disclaimer. Claims 1, 3-5 and 9-11 stand rejected. Therefore, Claims 1, 3-5 and 9-11 are being appealed in this Brief. A copy of the appealed claims is included in the Claims Appendix.

IV. STATUS OF AMENDMENTS

A non-final Office Action was mailed on February 24, 2010, in which the Examiner rejected Claims 1, 3-5 and 9-11 under 35 U.S.C. §112 and under 35 U.S.C. §103. Appellants filed a Response to the non-final Office Action on May 12, 2010, in which Appellants argued against the indefinite and obviousness rejections. A final Office Action was mailed on May 27, 2010, in which the Examiner maintained the rejections of Claims 1, 3-5 and 9-11 under 35 U.S.C. §112 and under 35 U.S.C. §103. Appellants filed a Notice of Appeal on August 6, 2010. Copies of the non-final Office Action and final Office Action are included in the Evidence Appendix as Exhibits A and B, respectively.

V. SUMMARY OF CLAIMED SUBJECT MATTER

A summary of the invention by way of reference to the specification (Preliminary Amendment) and/or figures for each of the independent claims is provided as follows:

Independent Claim 1 is directed to a natural lycopene concentrate that is water-soluble at room temperature (page 4, paragraph 9; page 6, paragraph 40) comprising at least 1 mg of lycopene per g of the said concentrate (page 4, paragraphs 15-16), not more than 30% proteins (page 4, paragraphs 15-16), not more than 30% polysaccharides (page 4, paragraphs 15-16), not more than 10% organic acids (page 4, paragraphs 15-16), and at least 30% of lipid compounds (page 4, paragraphs 15-16), wherein the concentrate is ingestible (page 7, paragraphs 46 and 48; Example 1), in powder form (page 6, paragraph 32) and isolated from fibers and other insoluble compounds by solid-liquid separation (page 6, paragraph 36), and wherein the concentrate is extracted from a lycopene-containing material without using a solvent (page 3, paragraph 7; page 5, paragraph 20).

Independent Claim 9 is directed to a cosmetic composition for slowing ageing of the skin and/or to combat skin damage which may be caused by exposure to ultraviolet light (page 7, paragraph 49), the composition comprising a natural lycopene concentrate that is water-soluble at room temperature (page 4, paragraph 9; page 6, paragraph 40) comprising at least 1 mg of lycopene per g of the said concentrate (page 4, paragraphs 15-16), not more than 30% of proteins (page 4, paragraphs 15-16), not more than 30% of polysaccharides (page 4, paragraphs 15-16), not more than 10% of organic acids (page 4, paragraphs 15-16), and at least 30% of lipid compounds containing at least $10^{-10}\%$ of lycopene (page 7, paragraph 45), wherein the concentrate is ingestible (page 7, paragraphs 46 and 48; Example 1), in powder form (page 6, paragraph 32) and isolated from fibers and other insoluble compounds by solid-liquid separation (page 6, paragraph 36), and wherein the concentrate is extracted from a lycopene-containing material without using a solvent (page 3, paragraph 7; page 5, paragraph 20).

Independent Claim 10 is directed to a composition which can be ingested orally in order to optimize the absorption of lycopene so as to induce photoprotection and thus slow ageing of the skin (page 7, paragraphs 43 and 49) comprising a natural lycopene concentrate that is water-soluble at room temperature (page 4, paragraph 9; page 6, paragraph 40) comprising at least 1 mg of lycopene per g of the said concentrate (page 4, paragraphs 15-16), not more than 30% of

proteins (page 4, paragraphs 15-16), not more than 30% of polysaccharides (page 4, paragraphs 15-16), not more than 10% of organic acids (page 4, paragraphs 15-16), and at least 30% of lipid compounds (page 4, paragraphs 15-16), wherein the concentrate is ingestible (page 7, paragraphs 46 and 48; Example 1), in powder form (page 6, paragraph 32) and isolated from fibers and other insoluble compounds by solid-liquid separation (page 6, paragraph 36), and wherein the concentrate is extracted from a lycopene-containing material without using a solvent (page 3, paragraph 7; page 5, paragraph 20).

Independent Claim 11 is directed to a dietary supplement containing doses of 0.001 to 100% of a concentrate comprising a natural lycopene concentrate that is water-soluble at room temperature (page 4, paragraph 9; page 6, paragraph 40) comprising at least 1 mg of lycopene per g of the said concentrate (page 4, paragraphs 15-16), not more than 30% of proteins (page 4, paragraphs 15-16), not more than 30% of polysaccharides (page 4, paragraphs 15-16), not more than 10% of organic acids (page 4, paragraphs 15-16), and at least 30% of lipid compounds (page 4, paragraphs 15-16), wherein the concentrate is ingestible (page 7, paragraphs 46 and 48; Example 1), in powder form (page 6, paragraph 32) and isolated from fibers and other insoluble compounds by solid-liquid separation (page 6, paragraph 36), and wherein the concentrate is extracted from a lycopene-containing material without using a solvent (page 3, paragraph 7; page 5, paragraph 20).

Although specification citations are given in accordance with C.F.R. 1.192(c), these reference numerals and citations are merely examples of where support may be found in the specification for the terms used in this section of the Brief. There is no intention to suggest in any way that the terms of the claims are limited to the examples in the specification. As demonstrated by the references numerals and citations below, the claims are fully supported by the specification as required by law. However, it is improper under the law to read limitations from the specification into the claims. Pointing out specification support for the claim terminology as is done here to comply with rule 1.192(c) does not in any way limit the scope of the claims to those examples from which they find support. Nor does this exercise provide a mechanism for circumventing the law precluding reading limitations into the claims from the specification. In short, the references numerals and specification citations are not to be construed as claim limitations or in any way used to limit the scope of the claims.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Claims 1, 3-5 and 9-11 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
2. Claims 1, 3-5 and 9-11 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,224,876 to Kesharlal et al. ("Kesharlal"). A copy of *Kesharlal* is included in the Evidence Appendix as Exhibit C.

VII. ARGUMENT

A. LEGAL STANDARDS

1. Definiteness under 35 U.S.C. §112, second paragraph

The standard for determining whether the definitiveness requirement is met under 35 U.S.C. § 112, ¶ 2 is “whether those skilled in the art would understand what is claimed when the claim is read in light of the Specification.” *Orthokinetics Inc. v. Safety Travel Chairs Inc.*, 1 U.S.P.Q. 2d 1081-1088 (Fed. Cir. 1986). “If the claims, read in light of the Specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the Courts can demand no more.” *North American Vaccine Inc. v American Cyanamid Co.*, 28 U.S.P.Q. 2d 1333, 1339 (Fed. Cir. 1993). In this regard, “[p]atent law allows the inventor to be his own lexicographer ... [T]he specification aids in ascertaining the scope and meaning of the language employed in the claims inasmuch as words must be used in the same way in both the claims and the specification. *United States v. Teletronics, Inc.*, 8 U.S.P.Q. 2d 1217, 1220 (Fed. Cir. 1988). By statute, 35 U.S.C. 112, Congress has placed no limitations on how an applicant claims his invention, so long as the specification concludes with claims which particularly point out and distinctly claim that invention.” *In re Pilkington*, 162 U.S.P.Q. 145, 148 (C.C.P.A. 1996).

2. Obviousness under 35 U.S.C. §103

The Federal Circuit has held that the legal determination of an obviousness rejection under 35 U.S.C. § 103 is:

whether the claimed invention as a whole would have been obvious to a person of ordinary skill in the art at the time the invention was made...The foundational facts for the *prima facie* case of obviousness are: (1) the scope and content of the prior art; (2) the difference between the prior art and the claimed invention; and (3) the level of ordinary skill in the art...Moreover, objective indicia such as commercial success and long felt need are relevant to the determination of obviousness...Thus, each obviousness determination rests on its own facts.

In re Mayne, 41 U.S.P.Q. 2d 1451, 1453 (Fed. Cir. 1997).

In making this determination, the Patent Office has the initial burden of proving a *prima facie* case of obviousness. *In re Rijckaert*, 9 F.3d 1531, 1532, 28 U.S.P.Q. 2d 1955, 1956 (Fed.

Cir. 1993). This burden may only be overcome “by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings.” *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q. 2d 1596, 1598 (Fed. Cir. 1988). “If the examination at the initial stage does not produce a *prima facie* case of unpatentability, then without more the applicant is entitled to grant of the patent.” *In re Oetiker*, 24 U.S.P.Q. 2d 1443, 1444 (Fed. Cir. 1992).

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference or references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Fine*, 837 F.2d 1071, 5, U.S.P.Q.2d 1596 (Fed. Cir. 1988). Second, there must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 U.S.P.Q. 375 (Fed. Cir. 1986). Finally, all of the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q., 580 (CCPA 1974).

Further, the Federal Circuit has held that it is “impermissible to use the claimed invention as an instruction manual or ‘template’ to piece together the teachings of the prior art so that the claimed invention is rendered obvious.” *In re Fritch*, 23 U.S.P.Q.2d 1780, 1784 (Fed. Cir. 1992). “One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.” *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988).

Moreover, the Federal Circuit has held that “obvious to try” is not the proper standard under 35 U.S.C. §103. *Ex parte Goldgaber*, 41 U.S.P.Q.2d 1172, 1177 (Fed. Cir. 1996). “An-obvious-to-try situation exists when a general disclosure may pique the scientist curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued.” *In re Eli Lilly and Co.*, 14 U.S.P.Q.2d 1741, 1743 (Fed. Cir. 1990).

Of course, references must be considered as a whole and those portions teaching against or away from the claimed invention must be considered. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve Inc.*, 796 F.2d 443 (Fed. Cir. 1986). “A prior art reference may be considered to teach away when a person of ordinary skill, upon reading the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the Applicant.” *Monarch Knitting Machinery Corp. v. Fukuhara*

Industrial Trading Co., Ltd., 139 F.3d 1009 (Fed. Cir. 1998), quoting, *In re Gurley*, 27 F.3d 551 (Fed. Cir. 1994).

B. THE CLAIMED INVENTION

Independent Claim 1 is directed to a natural lycopene concentrate that is water-soluble at room temperature. The concentrate includes at least 1 mg of lycopene per g of the said concentrate, not more than 30% proteins, not more than 30% polysaccharides, not more than 10% organic acids, and at least 30% of lipid compounds. The concentrate is ingestible, in powder form and is isolated from fibers and other insoluble compounds by solid-liquid separation. The concentrate is also extracted from a lycopene-containing material without using a solvent.

Independent Claim 9 is directed to a cosmetic composition for slowing ageing of the skin and/or to combat skin damage which may be caused by exposure to ultraviolet light. The composition includes a natural lycopene concentrate that is water-soluble at room temperature, and has at least 1 mg of lycopene per g of the said concentrate, not more than 30% of proteins, not more than 30% of polysaccharides, not more than 10% of organic acids, and at least 30% of lipid compounds containing at least $10^{-10}\%$ of lycopene. The concentrate is ingestible, in powder form and is isolated from fibers and other insoluble compounds by solid-liquid separation. The concentrate is extracted from a lycopene-containing material without using a solvent.

Independent Claim 10 is directed to a composition that can be ingested orally in order to optimize the absorption of lycopene so as to induce photoprotection and thus slow ageing of the skin. The composition includes a natural lycopene concentrate that is water-soluble at room temperature, and has at least 1 mg of lycopene per g of the said concentrate, not more than 30% of proteins, not more than 30% of polysaccharides, not more than 10% of organic acids, and at least 30% of lipid compounds. The concentrate is ingestible, in powder form and is isolated from fibers and other insoluble compounds by solid-liquid separation. The concentrate is extracted from a lycopene-containing material without using a solvent.

Independent Claim 11 is directed to a dietary supplement containing doses of 0.001 to 100% of a concentrate that includes a natural lycopene concentrate that is water-soluble at room temperature and has at least 1 mg of lycopene per g of the said concentrate, not more than 30%

of proteins, not more than 30% of polysaccharides, not more than 10% of organic acids, and at least 30% of lipid compounds. The concentrate is ingestible, in powder form and is isolated from fibers and other insoluble compounds by solid-liquid separation. The concentrate is extracted from a lycopene-containing material without using a solvent.

C. CLAIMS 1, 3-5 AND 9-11 ARE SUFFICIENTLY DEFINITE TO SATISFY THE REQUIREMENTS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

The standard for determining whether the definitiveness requirement is met under 35 U.S.C. §112, second paragraph, is whether those skilled in the art would understand what is claimed when the claim is read in light of the specification. With respect to the presently claimed subject matter, Appellants respectfully disagree with the Examiner's assertion the phrase "natural lycopene concentrate" is unclear. See, final Office Action, pages 2-4. Instead, Appellants respectfully submit that the skilled artisan would immediately understand the scope of the claims when read in view of the specification.

As is clearly stated in the specification, "[t]he aim of the present invention is to provide a 'natural' product with increased bioavailability, that is to say that the product has only been subjected to technological treatments which do not modify its native characteristics." See, specification, page 3, paragraph 7 (emphasis added). The specification further states that "the process of extraction according to the invention is simple, rapid and economical and at no time subject to the state of viability of the endoenzymes of the raw material." See, specification, page 4, paragraph 8. As such, the skilled artisan would immediately appreciate that a "natural" lycopene concentrate is a lycopene concentrate that has not be subjected to technological treatments that would modify its native characteristics. Indeed, the specification clearly defines a "natural" lycopene concentrate as a lycopene concentrate that "has only been subjected to technological treatments which do not modify its native characteristics." Thus, not only is the phrase "natural lycopene concentrate" explicitly defined in the specification, but the skilled artisan would immediately appreciate what it means to modify the native characteristics of a lycopene concentrate.

The Examiner asserts that "[t]he term 'natural' is not defined by the claims" and states that since "[Appellant] recites '[t]he supernatant is recovered and its pH is adjusted to 7 with

NaOH,”” and “NaOH does not exist in nature[al] tomato,” people would not consider the presently claimed lycopene concentrates to be “natural.” See, final Office Action, pages 2-4. Appellants respectfully disagree.

In contrast, Appellants submit that a “natural product” is, in fact, defined in the specification. As stated above, the specification clearly states that “[t]he aim of the present invention is to provide a ‘natural’ product with increased bioavailability, that is to say that the product has only been subjected to technological treatments which do not modify its native characteristics.” See, specification, page 3, paragraph 7 (emphasis added). Thus, the skilled artisan would appreciate the meaning of “natural” lycopene based on the express definition of a “natural” product.

Further, the Manual for Patent Examining Procedures (“MPEP”) and case law precedent have found time and again that an applicant for patent may be her own lexicographer. Indeed, the Federal Circuit has found that “[p]atent law allows the inventor to be his own lexicographer . . . [T]he specification aids in ascertaining the scope and meaning of the language employed in the claims inasmuch as words must be used in the same way in both the claims and the specification. *United States v. Teletronics, Inc.*, 8 U.S.P.Q. 2d 1217, 1220 (Fed. Cir. 1988). As such, Appellants may define “natural” in any manner desired. “By statute . . . Congress has placed no limitations on how an applicant claims his invention, so long as the specification concludes with claims which particularly point out and distinctly claim that invention.” *In re Pilkington*, 162 U.S.P.Q. 145, 148 (C.C.P.A. 1996). Therefore, in contrast to the Examiner’s suggestion, there exists no requirement for patentability that Appellants must define terms to mean what “most people” would expect the term to mean. Moreover, Appellants have chosen a definition of the term “natural” that Appellants submit corresponds with a skilled artisan’s understanding of the term. Indeed, it seems logical that a “natural” product would not have been subject to technological treatments that would modify it’s native characteristics.

Moreover, Appellants respectfully submit that it does not matter if the pH of a solution is adjusted to 7 with NaOH, as is suggested by the Examiner. See, final Office Action, pages 2-3. Instead, Appellants submit that when the claims are read in view of the specification, the skilled artisan would immediately appreciate that using NaOH to alkalinze a lycopene-containing composition, or acidifying a filtrate prior to centrifugation clearly does not change the native characteristics of the ultimate lycopene-containing composition because, as discussed above, the

lycopene concentrate “has only been subjected to technological treatments which do not modify its native characteristics.” As such, the skilled artisan would understand that the alkalinization and acidification steps described in the specification do not change that the lycopene concentrates are “natural.”

As a result, the metes and bounds of the phrase “natural lycopene concentrate” are clear to the skilled artisan in view of the specification, the knowledge of the skilled artisan, as well as commonly used definitions of the terms. For at least the above mentioned reasons, Appellants respectfully submit that Claims 1, 3-5 and 9-11 fully comply with the requirements under 35 U.S.C. §112, second paragraph.

Accordingly, Appellants respectfully request that the indefiniteness rejection of Claims 1, 3-5 and 9-11 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

D. THE OBVIOUSNESS REJECTION OF CLAIMS 1, 3-5 AND 9-11 UNDER 35 U.S.C. §103(a) SHOULD BE REVERSED

Appellants respectfully submit that the obviousness rejection of Claims 1, 3-5 and 9-11 should be reconsidered and reversed because the Examiner has failed to establish a *prima facie* case of obviousness. In the final Office Action, the Examiner asserts that *Kesharlal* renders the claimed subject matter obvious. See, final Office Action, pages 4-9. However, the Examiner has failed to establish a *prima facie* case of obviousness because *Kesharlal* fails to disclose each and every element of the present claims. In addition, the skilled artisan would have no reason to modify *Kesharlal* to arrive at the present claims because *Kesharlal* teaches away from the present claims.

1. *Kesharlal* Fails to Disclose or Suggest Each and Every Element of the Present Claims

Independent Claims 1 and 10-11 recite, in part, natural lycopene concentrates comprising at least 1 mg of lycopene per g of the said concentrate, not more than 30% proteins, not more than 30% polysaccharides, not more than 10% organic acids, and at least 30% of lipid compounds, wherein the concentrate is ingestible, in powder form and isolated from fibers and

other insoluble compounds by solid-liquid separation, and wherein the concentrate is extracted from a lycopene-containing material without using a solvent.

As discussed in the specification, the presently claimed compositions contain natural lycopene concentrates having increased bioavailability. The increased bioavailability may be explained by the smaller size of the concentrate crystals that are obtained during processing. For example, the crystals obtained by the processes of the present specification are about 5 to 10 sizes smaller than those of the crystalline forms of oleoresin. Additionally, the raw lycopene materials used are more bioavailable because the technological treatments used to obtain the concentrate do not modify the native characteristics of the lycopene. See, specification, page 3, paragraph 7; page 5, paragraph 21. In contrast, Appellants respectfully submit that *Kesharlal* fails to disclose or suggest every element of the present claims.

For example, *Kesharlal* fails to disclose or suggest natural lycopene concentrates comprising at least 1 mg of lycopene per g of the said concentrate, not more than 30% proteins, not more than 30% polysaccharides, not more than 10% organic acids, and at least 30% of lipid compounds, wherein the concentrate is ingestible, in powder form and isolated from fibers and other insoluble compounds by solid-liquid separation, and wherein the concentrate is extracted from a lycopene-containing material without using a solvent as required, in part, by independent Claims 1 and 10-11, and as is admitted by the Examiner. See, final Office Action, page 8, lines 1-3 and 9-10. Instead, *Kesharlal* is entirely directed to pharmacologically and biologically active compositions containing carotenoids, micro- and macro-nutrients and a process for their preparation from carrots. See, *Kesharlal*, Abstract; column 1, lines 8-12. At best, *Kesharlal* discloses a composition containing 10-50 g proteins per 100 g of isolated powder for carrots. See, *Kesharlal*, column 4, lines 27-39. Every specific example in *Kesharlal*, other than the range of amounts for carrots, uses an amount of proteins that is greater than 30%. See, *Kesharlal*, Examples 1-2 and 4-14.

For at least the above-mentioned reasons, Appellants respectfully submit that *Kesharlal* is deficient with respect to the present claims.

Accordingly, Appellants respectfully request that the obviousness rejection of Claims 1, 3-5 and 9-11 under 35 U.S.C. §103(a) be reconsidered and reversed.

2. The Skilled Artisan Would Have No Reason to Modify *Kesharlal* to Arrive at the Present Claims

Appellants further submit that the skilled artisan would have no reason to modify *Kesharlal* to arrive at the present claims because *Kesharlal* teaches away from the present claims. As discussed above, independent Claims 1 and 10-11 recite, in part, natural lycopene concentrates comprising at least 1 mg of lycopene per g of the said concentrate, not more than 30% proteins, not more than 30% polysaccharides, not more than 10% organic acids, and at least 30% of lipid compounds. As such, the claims are directed to natural concentrates that cannot include more than 30% proteins.

In the final Office Action, the Examiner admits that *Kesharlal* fails to disclose or suggest not more than 30% protein, but states that because *Kesharlal* “teaches a protein range from about 10-50% protein, which overlaps with the claimed [amount of protein].” See, final Office Action, page 8, lines 11-12. However, Appellants respectfully disagree and submit that not only does *Kesharlal* fails to disclose or suggest the natural lycopene concentrates of the present claims, but *Kesharlal* teaches away from the presently claimed amounts of protein.

For example, and as admitted by the Examiner, *Kesharlal* fails to disclose or suggest concentrates containing not more than 30% protein as required, in part, by the present claims. Indeed, since *Kesharlal* “teaches a protein range from about 10-50%,” *Kesharlal* clearly discloses that protein amounts in the range of 30-50% are acceptable. However, this is in direct contrast to the present claims that explicitly require “no more than 30% proteins.” As such, the disclosure of *Kesharlal* clearly teaches away from the present claims.

The Examiner goes further to state that “*Kesharlal* does not ‘teach away’ from the claimed invention, as it does not say ‘more than 30% of the protein will not work.’” See, final Office Action, page 8, lines 15-16. However, Appellants respectfully disagree and submit that such an explicit disparagement is not required in order for a reference to teach away from a claimed invention. Indeed, the presence of 30-50% protein in the composition of *Kesharlal* is not merely the disclosure of an alternative embodiment. Rather, the presence of 30-50% protein in the compositions of *Kesharlal* teaches that such amounts of protein are not only acceptable, but also preferred. See, *Kesharlal*, Examples. In contrast, the present claims clearly require the

opposite conclusion that more than 30% protein is not an acceptable amount. As such, Appellants submit that the disclosure of *Kesharlal* clearly teaches away from the present claims.

For at least the above-mentioned reasons, Appellants respectfully submit that *Kesharlal* is deficient with respect to the present claims.

Accordingly, Appellants respectfully request that the obviousness rejection of Claims 1, 3-5 and 9-11 under 35 U.S.C. §103(a) to *Kesharlal* be reconsidered and reversed.

VIII. CONCLUSION

Appellants respectfully submit that the Examiner has failed to establish either indefiniteness or a *prima facie* case of obviousness under 35 U.S.C. §103 with respect to the present claims. Accordingly, Appellants respectfully submit that the indefiniteness and obviousness rejections are erroneous in law and in fact and should, therefore, be reversed by this Board.

The Director is authorized to charge \$540 for the Appeal Brief and any additional fees which may be required, or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 3712036-00706 on the account statement.

Respectfully submitted,

K&L GATES LLP

BY

Robert M. Barrett
Reg. No. 30,142
Customer No. 29157
Phone No. 312-807-4204

Dated: September 29, 2010

CLAIMS APPENDIX

PENDING CLAIMS ON APPEAL OF U.S. PATENT APPLICATION SERIAL NO. 10/568,704

1. A natural lycopene concentrate that is water-soluble at room temperature comprising at least 1 mg of lycopene per g of the said concentrate, not more than 30% proteins, not more than 30% polysaccharides, not more than 10% organic acids, and at least 30% of lipid compounds, wherein the concentrate is ingestible, in powder form and isolated from fibers and other insoluble compounds by solid-liquid separation, and wherein the concentrate is extracted from a lycopene-containing material without using a solvent.
3. The concentrate according to Claim 1, comprising a vitamin selected from the group consisting of vitamin E, vitamin C, and combinations thereof.
4. The concentrate according to Claim 1, comprising between 1 mg and 40 mg of lycopene per g of concentrate.
5. The concentrate according to Claim 1, comprising between 10 and 30 mg of lycopene per g of concentrate.
9. A cosmetic composition for slowing ageing of the skin and/or to combat skin damage which may be caused by exposure to ultraviolet light, the composition comprising a natural lycopene concentrate that is water-soluble at room temperature comprising at least 1 mg of lycopene per g of the said concentrate, not more than 30% of proteins, not more than 30% of polysaccharides, not more than 10% of organic acids, and at least 30% of lipid compounds containing at least $10^{-10}\%$ of lycopene, wherein the concentrate is ingestible, in powder form and isolated from fibers and other insoluble compounds by solid-liquid separation, and wherein the concentrate is extracted from a lycopene-containing material without using a solvent.

10. A composition which can be ingested orally in order to optimize the absorption of lycopene so as to induce photoprotection and thus slow ageing of the skin comprising a natural lycopene concentrate that is water-soluble at room temperature comprising at least 1 mg of lycopene per g of the said concentrate, not more than 30% of proteins, not more than 30% of polysaccharides, not more than 10% of organic acids, and at least 30% of lipid compounds, wherein the concentrate is ingestible, in powder form and isolated from fibers and other insoluble compounds by solid-liquid separation, and wherein the concentrate is extracted from a lycopene-containing material without using a solvent.

11. A dietary supplement containing doses of 0.001 to 100% of a concentrate comprising a natural lycopene concentrate that is water-soluble at room temperature comprising at least 1 mg of lycopene per g of the said concentrate, not more than 30% of proteins, not more than 30% of polysaccharides, not more than 10% of organic acids, and at least 30% of lipid compounds, wherein the concentrate is ingestible, in powder form and isolated from fibers and other insoluble compounds by solid-liquid separation, and wherein the concentrate is extracted from a lycopene-containing material without using a solvent.

EVIDENCE APPENDIX

EXHIBIT A: Non-final Office Action dated February 24, 2010

EXHIBIT B: Final Office Action dated May 27, 2010

EXHIBIT C: U.S. Patent No. 6,224,876 to Kesharlal et al. ("Kesharlal")

RELATED PROCEEDINGS APPENDIX

None.

EXHIBIT A



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,704	02/16/2006	Karlheinz Bortlik	3712036.00706	4852
29157	7590	02/24/2010	EXAMINER	
K&L Gates LLP P.O. Box 1135 CHICAGO, IL 60690				MI, QIUWEN
ART UNIT		PAPER NUMBER		
		1655		
NOTIFICATION DATE		DELIVERY MODE		
02/24/2010		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chicago.patents@klgates.com

Office Action Summary	Application No.	Applicant(s)	
	10/568,704	BORTLIK ET AL.	
	Examiner	Art Unit	
	QIUWEN MI	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 29 January 2010.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,3-12,14 and 15 is/are pending in the application.
 - 4a) Of the above claim(s) 6-8,12,14 and 15 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1,3-5 and 9-11 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

CONTINUED EXAMINATIONS

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/29/2010 has been entered.

Applicant's amendment in the reply filed on 1/29/2010 is acknowledged. Claims 2 and 13 are cancelled. Claims 1, 3-12, 14, and 15 are pending. Claims 6-8, 12, 14, and 15 are withdrawn as they are directed toward a non-elected invention group. **Claims 1, 3-5, and 9-11 are examined on the merits.**

Any rejection that is not reiterated is hereby withdrawn.

Claim Rejections –35 USC § 112, 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-5, and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 (line 1), 9 (line 3), 10 (line 3), and 11 (line 2) recite "natural lycopene concentrate". The term "natural lycopene concentrate" in claims 1, and 9-11 is a relative term

Art Unit: 1655

which renders the claim indefinite. The term "natural" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For instance, on page 8 of the specification, Applicant recites "The supernatant is recovered and its pH is adjusted to 7 with NaOH" (lines 5-10). Since NaOH does not exist in nature tomato, it is not clear whether the product could still be called "natural lycopene concentrate".

Thus, the metes and bounds of claims 1, and 9-11 are rendered uncertain by the phrase "natural lycopene concentrate" in claims 1, and 9-11 because "natural" could be a relative term.

All other cited claims depend directly or indirectly from rejected claims and are, therefore, also, rejected under U.S.C. 112, second paragraph for the reasons set forth above.

Claim Rejections –35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-5, and 9-11 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Kesharlal et al (US 6,224,876).

This is a new rejection necessitated by the Applicant's amendment filed on 1/29/2010.

Kesharlal et al teach fresh hard, good quality reddish colored "Desi Red" carrots with a smooth surface, excluding those that were found defective, were selected and washed thoroughly

with water. The sorted and washed carrots (1.0 kg) were subjected to crushing in a fruit mill to provide a comminution which was subjected to pressing through a filter press for the purpose of separating the pulp from the juice to provide a juice (ca. 600 ml) (thus water soluble at room temperature, thus the concentrate is extracted from a lycopene-containing material without using a solvent, thus a solid-liquid separation). To the juice, 3 g of adipic acid was added with stirring (thus not more than 10% organic acid). To the resulting mixture was added 60 g of sorbitol and the mixture was subjected to centrifuging to provide paste (ca. 17.2 g). The paste was dried under high vacuum. Pulverizing of the solid material and sieving gave the carotenoid powder of the invention (3.8 g) (col 7, Example 1). The composition of the product is given below.

Composition per 100 g product from "Desi Red" carrots (Example 1): beta-Carotene 530 mg; alpha-Carotene 27 mg, Lycopene 700 mg (thus 7 mg/g; thus at least 1 mg of lycopene per g); Lutein/Xeaxanthin 15 mg; Total Carotenoids 3750 mg; Proteins 32.8 g (thus 32.8%); Carbohydrates 4 g; Phosphorus 647 mg; Lipids 15.3 g (thus 15.3%); Vitamin C 22 mg; Vitamin B1 5 mg; Vitamin B2 1 mg; Iron 95 mg; Zinc 1 mg; Manganese 1 mg; Magnesium 162 mg; Calcium 1.381 g; Potassium 1.99 g; Sodium 1.99 g; Total Minerals (Ash value) 6.87 g (col 8, 1st table). In Example 2, Kesharlal et al also teach the "Bangalore local" carrots were processed according the procedure described in Example 1. Composition per 100g product from "Bangalore local" carrots contain 30.3 g lipids (thus at least 30% lipid compounds), and protein 31.5 g (thus 31.5%). Even though Kesharlal et al do not explicitly teach not more than 30% protein, in Example 3, Kesharlal et al teach the protein range from different supplies contain 10-50% protein. Kesharlal et al further teach 5 participants sensitive to continuous exposure to sunlight and suffering from skin erythema on longer exposure were administered the tablets over

Art Unit: 1655

a period of four weeks. Significant reduction of the symptoms induced by long exposure were observed (col 12, lines 20-25) (thus a cosmetic composition (that is taken orally) for slowing aging of the skin and/or to combat skin damage which may be caused by exposure to ultraviolet light). Kesharlal et al further teach the tablets (thus a composition which can be ingested orally, thus a dietary supplement) were prepared by blending nutrient-rich carotenoid powder with sucrose and Microcrystalline cellulose, granulating with Starch Gelatin paste, drying, lubricating with Talc, Magnesium stearate and Colloidal silicon dioxide followed by compression into tablet (col 10, lines 15-20).

Kesharlal et al do not explicitly teach a natural lycopene concentrate containing not more than 30% protein.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to vary the amount of the protein in a natural lycopene concentrate since in Example 3, Kesharlal et al teach different supplies contain 10-50% protein. Therefore, it would have been obvious for one of the ordinary skill in the art to choose a particular protein content carrot from different carrot species or supplier. Since Kesharlal et al yielded beneficial results for producing lycopene containing product, one of ordinary skill in the art would have been motivated to make and use the invention.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Art Unit: 1655

Applicant's arguments, regarding the cited references do not teach ingestible powder form, have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Kesharla et al.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Qiuwen Mi/

Application/Control Number: 10/568,704

Art Unit: 1655

Page 7

Examiner, Art Unit 1655

Notice of References Cited		Application/Control No.	Applicant(s)/Patent Under Reexamination BORTLIK ET AL.	
		Examiner QIUWEN MI	Art Unit 1655	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-6,224,876	05-2001	Kesharlal et al.	424/773
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

EXHIBIT B



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,704	02/16/2006	Karlheinz Bortlik	3712036.00706	4852
29157	7590	05/27/2010	EXAMINER	
K&L Gates LLP P.O. Box 1135 CHICAGO, IL 60690				MI, QIUWEN
ART UNIT		PAPER NUMBER		
		1655		
NOTIFICATION DATE		DELIVERY MODE		
05/27/2010		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chicago.patents@klgates.com

Office Action Summary	Application No.	Applicant(s)	
	10/568,704	BORTLIK ET AL.	
	Examiner	Art Unit	
	QIUFEN MI	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 12 May 2010.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,3-12,14 and 15 is/are pending in the application.
- 4a) Of the above claim(s) 6-8,12,14 and 15 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1, 3-5, and 9-11 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ . | 6) <input type="checkbox"/> Other: _____ . |

Concentrate that DETAILED ACTION

Applicant's reply filed on 5/12/2010 is acknowledged. Claims 2 and 13 are cancelled.

Claims 1, 3-12, 14, and 15 are pending. Claims 6-8, 12, 14, and 15 are withdrawn as they are directed toward a non-elected invention group. **Claims 1, 3-5, and 9-11 are examined on the merits.**

Any rejection that is not reiterated is hereby withdrawn.

Claim Rejections –35 USC § 112, 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-5, and 9-11 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is maintained for reasons of record set forth in the Office Action mailed out on 2/24/2010, repeated below. Applicants' arguments filed have been fully considered but they are not deemed to be persuasive.

Claims 1 (line 1), 9 (line 3), 10 (line 3), and 11 (line 2) recite "natural lycopene concentrate". The term "natural lycopene concentrate" in claims 1, and 9-11 is a relative term which renders the claim indefinite. The term "natural" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. For instance, on page 8 of the specification, Applicant recites "The supernatant is recovered and its

Art Unit: 1655

pH is adjusted to 7 with NaOH" (lines 5-10). Since NaOH does not exist in nature tomato, it is not clear whether the product could still be called "natural lycopene concentrate".

Thus, the metes and bounds of claims 1, and 9-11 are rendered uncertain by the phrase "natural lycopene concentrate" in claims 1, and 9-11 because "natural" could be a relative term.

All other cited claims depend directly or indirectly from rejected claims and are, therefore, also, rejected under U.S.C. 112, second paragraph for the reasons set forth above.

Applicant argues that "As is clearly stated in the specification, "[t]he aim of the present invention is to provide a 'natural' product with increase bioavailability, that is to say that the product has only been subjected to technological treatments which do not modify its native characteristics." See, specification (Preliminary Amendment), page 3, paragraph 7. The specification further states that "the process of extraction according to the invention is simple, rapid and economical and at no time subject to the state of viability of the endoenzymes of the raw material." See, specification, page 4, paragraph 8. As such, the skilled artisan would immediately appreciate that a "natural" lycopene concentrate is a lycopene concentrate that has not been subjected to technological treatments that would modify its native characteristics. Indeed, the specification clearly defines a "natural" lycopene concentrate as a lycopene concentrate that "has only been subjected to technological treatments which do not modify its native characteristics." Thus, not only is the phrase "natural lycolSene concentrate" explicitly defined in the specification, but the skilled artisan would immediately appreciate what it means to modify the native characteristics of a lycopene concentrate. For at least the above mentioned reasons,

Art Unit: 1655

Applicants respectfully submit that Claims 1, 3-5 and 9-11 fully comply with the requirements under 35 U.S.C. §112, second paragraph" (page 2, last paragraph bridging page 3).

This is not found persuasive. As indicated in the last Office Action, "natural" is a relative term, people might consider that only tomato concentrate going through squeezing or pressing procedure is considered as "natural", and most people would consider when "NaOH" is added to a tomato concentrate (see Specification, lines 5-10), it is not "natural", as a natural tomato doesn't contain NaOH solution. Therefore, the metes and bounds of claims 1, and 9-11 are rendered uncertain by the phrase "natural lycopene concentrate" in claims 1, and 9-11 because "natural" could be a relative term.

Claim Rejections –35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-5, and 9-11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kesharlal et al (US 6,224,876).

This rejection is maintained for reasons of record set forth in the Office Action mailed out on 2/24/2010, repeated below. Applicants' arguments filed have been fully considered but they are not deemed to be persuasive.

Art Unit: 1655

Kesharlal et al teach fresh hard, good quality reddish colored "Desi Red" carrots with a smooth surface, excluding those that were found defective, were selected and washed thoroughly with water. The sorted and washed carrots (1.0 kg) were subjected to crushing in a fruit mill to provide a comminution which was subjected to pressing through a filter press for the purpose of separating the pulp from the juice to provide a juice (ca. 600 ml) (thus water soluble at room temperature, thus the concentrate is extracted form a lycopene-containing material without using a solvent, thus a solid-liquid separation). To the juice, 3 g of adipic acid was added with stirring (thus not more than 10% organic acid). To the resulting mixture was added 60 g of sorbitol and the mixture was subjected to centrifuging to provide paste (ca. 17.2 g). The paste was dried under high vacuum. Pulverizing of the solid material and sieving gave the carotenoid powder (thus ingestible, thus in a powder form) of the invention (3.8 g) (col 7, Example 1). The composition of the product is given below. Composition per 100 g product from "Desi Red" carrots (Example 1): beta-Carotene 530 mg; alpha-Carotene 27 mg, Lycopene 700 mg (thus 7 mg/g; thus at least 1 mg of lycopene per g); Lutein/Xeaxanthin 15 mg; Total Carotenoids 3750 mg; Proteins 32.8 g (thus 32:8%); Carbohydrates 4 g; Phosphorus 647 mg; Lipids 15.3 g (thus 15.3%); Vitamin C 22 mg; Vitamin B1 5 mg; Vitamin B2 1 mg; Iron 95 mg; Zinc 1 mg; Manganese 1 mg; Magnesium 162 mg; Calcium 1.381 g; Potassium 1.99 g; Sodium 1.99 g; Total Minerals (Ash value) 6.87 g (col 8, 1st table). In Example 2, Kesharlal et al also teach the "Bangalore local" carrots were processed according the procedure described in Example 1. Composition per 100g product from "Bangalore local" carrots contain 30.3 g lipids (thus at least 30% lipid compounds), and protein 31.5 g (thus 31.5%). Even though Kesharlal et al do not explicitly teach not more than 30% protein, in Example 3, Kesharlal et al teach the protein range

Art Unit: 1655

from different supplies contain 10-50% protein. Kesharlal et al further teach 5 participants sensitive to continuous exposure to sunlight and suffering from skin erythema on longer exposure were administered the tablets over a period of four weeks. Significant reduction of the symptoms induced by long exposure were observed (col 12, lines 20-25) (thus a cosmetic composition (that is taken orally) for slowing aging of the skin and/or to combat skin damage which may be caused by exposure to ultraviolet light). Kesharlal et al further teach the tablets (thus a composition which can be ingested orally, thus a dietary supplement) were prepared by blending nutrient-rich carotenoid powder with sucrose and Microcrystalline cellulose, granulating with Starch Gelatin paste, drying, lubricating with Talc, Magnesium stearate and Colloidal silicon dioxide followed by compression into tablet (col 10, lines 15-20).

Kesharlal et al do not explicitly teach a natural lycopene concentrate containing not more than 30% protein.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to vary the amount of the protein in a natural lycopene concentrate since in Example 3, Kesharlal et al teach different supplies contain 10-50% protein. Therefore, it would have been obvious for one of the ordinary skill in the art to choose a particular protein content carrot from different carrot species or supplier. Since Kesharlal et al yielded beneficial results for producing lycopene containing product, one of ordinary skill in the art would have been motivated to make and use the invention.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Applicant argues that "For example, *Kesharlal* fails to disclose or suggest natural lycopene concentrates comprising at least 1 mg of lycopene per g of the said concentrate, not more than 30% proteins, not more than 30% polysaccharides, not more than 10% organic acids, and at least 30% of lipid compounds, wherein the concentrate is ingestible, in powder form and isolated from fibers and other insoluble compounds by solid-liquid separation, and wherein the concentrate is extracted from a lycopene-containing material without using a solvent as required, in part, by independent Claims 1 and 10-11. Instead, *Kesharlal* is entirely directed to pharmacologically and biologically active compositions containing carotenoids, micro and macro nutrients and a process for their preparation from carrots. See, *Kesharlal*, Abstract; column 1, lines 8-12" (page 3, last paragraph bridging page 4).

Applicant also argues that "The Patent Office admits that *Kesharlal* fails to disclose or suggest not more than 30% protein, but states that because *Kesharlal* "teaches a protein range from about 10-50% protein that it would have been obvious for one of ordinary skill in the art to choose a particular protein content carrot from [a] different carrot species or supplier." See, Office Action, page 4, line 19- page 5, line 15. However, Applicants respectfully disagree and submit that not only does *Kesharlal* fails to disclose or suggest the natural lycopene concentrates of the present claims, but *Kesharlal* teaches away from the presently claimed amounts of protein" (page 4, 2nd paragraph).

Applicant further argues that "For example, as admitted by the Patent Office, *Kesharlal* fails to disclose or suggest not more than 30% protein as required, in part, by the present claims. Indeed, since *Kesharlal* "teaches a protein range from about 10-50%," *Kesharlal* clearly discloses that protein amounts in the range of 30-50% are acceptable. However, this is in direct contrast to the present claims that explicitly require "no more than 30% proteins." As such, the disclosure of *Kesharlal* clearly teaches away from the present claims. For at least the above-mentioned reasons, Applicants respectfully submit that *Kesharlal* is deficient with respect to the present claims" (page 4, 3rd paragraph).

This is not found persuasive. First of all, *Kesharlal* teaches every limitation of the claims, except "not more than 30% protein". If *Kesharlal* teaches that part, it would be a 102 rejection, not a 103. Secondly, *Kesharlal* teaches a protein range from about 10-50%, which overlaps with the claimed "not more than 30% protein", and it would be obvious for one of the ordinary skills in the art to choose any concentration from that range, including "not more than 30% protein". Further more, *Kesharlal* does not "teach away" from the claimed invention, as it does not say, "more than 30% of the protein will not work". Applicant argues that the cited reference teaches away from the claimed invention. According to MPEP 2123, "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) (The invention was directed to an epoxy impregnated fiber-reinforced printed circuit material. The applied prior art reference taught a printed circuit

material similar to that of the claims but impregnated with polyester-imide resin instead of epoxy. The reference, however, disclosed that epoxy was known for this use, but that epoxy impregnated circuit boards have “relatively acceptable dimensional stability” and “some degree of flexibility,” but are inferior to circuit boards impregnated with polyester-imide resins. The court upheld the rejection concluding that applicant’s argument that the reference teaches away from using epoxy was insufficient to overcome the rejection since “Gurley asserted no discovery beyond what was known in the art.” 27 F.3d at 554, 31 USPQ2d at 1132.). Furthermore, “[t]he prior art’s mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed....” In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004).

Applicant's arguments have been fully considered but they are not persuasive, and therefore the rejections in the record are maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Qiuwen Mi/

Examiner, Art Unit 1655

EXHIBIT C



US006224876B1

(12) **United States Patent**
Kesharlal et al.

(10) **Patent No.:** US 6,224,876 B1
(45) **Date of Patent:** May 1, 2001

(54) **ISOLATION AND FORMULATIONS OF NUTRIENT-RICH CAROTENOIDS**

(76) Inventors: **Biyani Milind Kesharlal**, 11, Shivam, Malbar Hill Road, Mumbai-400 082; **Simha Nanda Pratap**, Kaustubh Society, Block No. 9, Adarsh, Nagar, Kopri, Thane, (E)-400603; **Biyani Sushma Milind**, 11, Shivam, Malbar Hill Road, Mumbai-400 082; **Nunes Priya Ann**, 23A, St. Dominic's Road, Mumbai-400 050; **Gupta Sanjay Harnarayan**, 4, Radhabai Building, Pandit Solicitor Lane, Rani Sati Marg, Mumbai-400 097, all of (IN)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: 09/460,118

(22) Filed: Dec. 13, 1999

Related U.S. Application Data

- (62) Division of application No. 09/130,350, filed on Aug. 4, 1998, now Pat. No. 6,056,962.
(51) Int. Cl.⁷ A61K 35/78
(52) U.S. Cl. 424/195.1
(58) Field of Search 424/195.1; 426/2

(56) **References Cited****U.S. PATENT DOCUMENTS**

2,567,362 *	9/1951	Berkman et al.	424/195.1
2,739,145 *	3/1956	Barnett	530/370
2,848,508 *	8/1958	Barnett et al.	585/803
5,245,095 *	9/1993	Graves et al.	585/351
5,292,538 *	3/1994	Paul et al.	426/74
5,476,678 *	12/1995	Walter et al.	426/660
5,549,905 *	8/1996	Mark et al.	424/439
5,589,468 *	12/1996	Lin et al.	514/52
5,641,531 *	6/1997	Liebrecht et al.	426/583
5,686,429 *	11/1997	Lin et al.	514/52
5,830,738 *	11/1998	Thomas et al.	435/209

* cited by examiner

Primary Examiner—Jean C. Witz

(74) Attorney, Agent, or Firm—Bierman, Muserlian and Lucas

(57) **ABSTRACT**

Pharmacologically and biologically active compositions containing carotenoids, in combination with micro and macro nutrients, a process for their preparation from carrots and their use in formulations for health care and nutrition applications. The process includes sequentially treating carrot juice with a carboxylic acid and a saccharide to obtain a carotenoid fraction rich in micro and macro nutrients in proportions compatible with those originally found in the natural state. A method of treating retinoid deficient states and immunomodulation is also disclosed using the composition.

8 Claims, No Drawings

1**ISOLATION AND FORMULATIONS OF
NUTRIENT-RICH CAROTENOIDS**

This is a Division of Ser. No. 09/130,350 filed Aug. 4, 1998 now U.S. Pat. No. 6,056,962.

FIELD OF THE INVENTION

The invention relates to pharmacologically and biologically active compositions containing carotenoids, micro and macro nutrients, a process for their preparation from carrots and their use in formulations for health care and nutrition applications.

BACKGROUND OF THE INVENTION

Carotenoids are a class of naturally-occurring yellow, orange or red tetraterpenoids, found in traces in plant tissue, algae, bacteria and fungi. In particular they are found in vegetable sources such as carrots, spinach, tomatoes and fruits, such as, mango, peach, pumpkin, papaya. The more commonly known carotenoids are, alpha-carotene, beta-carotene, lutein, zeaxanthin, lycopene and cryptoxanthin.

Carotenoids possess significant nutritional value, carotenes and cryptoxanthin being considered as a provitamin A precursor for the formation of retinal and Vitamin A in humans. Vitamin A, an essential vitamin, for life is not synthesized in the animal cell.

Because carotenoids occur naturally in only trace amounts, the carotenoids must be extracted in concentrated form in order to be useful. Further carotenoids are sensitive to oxygen, air, heat and light.

Nutritionists advocate the daily use of carrots apart from other fresh vegetables and fruits in diet. Carrots are grown seasonally and good quality carrots are not available throughout the year at affordable prices. A little advertised fact about carrots is that only 20% of the total carotenes present are absorbed even when carrots are eaten in a finely grated form. The percentage of absorption from coarsely grated raw or cooked carrots is still less being around 5%.

The low absorption is attributed to the poor permeability of the cellulosic cell wall to carotenes even after cooking with the result that the major part remains enclosed within the cells. Hence as a source for deriving Vitamin A and use by themselves, carotenoid supplements free from cellulose are strongly recommended. Another advantage of using provitamin A carotenoids is that indiscriminate use of Vitamin A leads to serious toxic effects (Hypervitaminosis) whereas even in large doses carotenoids are harmless.

U.S. Pat. No. 2,567,362 describes fractional centrifugation process for the separation of colloidal dispersoids of active plant pigment units from the generated vegetable hydrosol.

U.S. Pat. No. 2,739,145 describes the separation of coagulated carotenoid-protein particles following heating of a suspension of the vegetable fibre-separated particles in vegetable serum.

U.K. patent 776,405 describes a carotene-concentrate used as a foodstuff for animals using calcium hydroxide and subsequent pH adjustment with phosphoric acid and then with formic acid.

U.S. Pat. No. 2,848,508 describes a process for recovery of carotene from carrots and provides a saturated solution of carotene in natural carrot oil from carrots.

WTO 86/04059 describes the use of a pectolytic enzyme followed by ultrafiltration for extracting and concentrating carotene.

2

U.S. Pat. No. 5,245,095 describes the use of calcium chloride, calcium hydroxide, calcium lactate or calcium gluconate to extract carotenoids from natural sources.

None of the above or any known processes provide a composition containing carotenoids in combination with micro and macro nutrients, the carotenoids being bound in moieties as in the natural source of carotenoids.

NATURE OF THE INVENTION

In recent times, carotenoids have been found in epidemiological observations to display protective activity as physiological antioxidants, thus reducing the risks of development of several chronic disorders such as heart diseases, cancer, cataract and other ailments. Holistic systems of medicine have, however, for centuries been advocating the synergistic value of dispensing not just pure but natural product ingredients. Use of pharmacologically or biologically active plant extracts is well-known.

Naturally occurring plant material contain a series of closely-related compounds produced naturally via biological and biochemical reactions. The plant is capable of producing a wide range of analogues at least one of which possesses the desired receptor compatibility. However, the related compounds appear to exercise a synergistic effect on the pharmacological or biological activity of the compatible compound and at the same time suppress toxic effects. Therefore the use of a composite set of nutrients as they are present in the natural source, is rapidly gaining supporters in modern medicine.

However, a major drawback in using plant material in its crude form or to use the plant material in its natural state, is that the dosages required of such material, to be therapeutically beneficial, are quite high. For example for receiving the therapeutic supply of carotenoids about one Kg of good quality carrots will have to be consumed every day. Such quantities cannot be conveniently converted into suitable dosage forms.

This invention, therefore, seeks to disclose a process for obtaining a pharmacologically or biologically active plant extract substantially as it occurs in its natural state suitable for converting in a convenient administrable dosage form. The process according to this invention, seeks to provide a concentrated plant extract, in which the plant extract comprises all pharmacologically or biologically active chemicals in the proportions as they exist in the original natural state without the use of organic solvents at any stage of its manufacture and avoiding the use of oils, enzymes, mineral acids, alkalis, metal salts and treatment by temperature in excess of 60 degrees celsius.

The advantage of naturally occurring series and analogues of compounds is achieved without compromising the overall effects of these compounds.

There is no report to date of a product which is standardised in respect of both the carotenoids content as well as the micro and macro nutrients with which the carotenoids are bound to and associated in its natural state occurring in vegetables, particularly carrots.

The present invention describes for the first time biologically or pharmacologically active material obtained from carrots, standardised with respect to its content of carotenoids, vitamins, proteins, lipids, carbohydrates, mineral and trace elements.

The present invention also describes a process to obtain the said material from carrots, which process comprises the addition of a carboxylic acid as herein defined to appropri-

ately processed carrots, followed by the addition of a carbohydrate as herein defined, separation of a carotenoids-rich paste, and subsequent drying.

The present invention also describes the use of the biologically or pharmacologically active material in the preparation of formulations for health care and nutrition applications for use in as variety of prophylactic and therapeutic conditions.

SUMMARY OF THE INVENTION

According to this invention there is provided a pharmacologically and biologically active composition extracted from carrots, including 0.25-5% mass as a percentage of total mass of extract of active carotenoid fraction, absorbable by an animal or human body in a convenient dosage form, in combination with micro and macro nutrients aiding in the absorption, assimilation and supplementing the action of the carotenoid fraction.

Typically, the carotenoid fraction includes alpha-carotene, beta-carotene, lutein, zeaxanthin and lycopene.

Typically the micro nutrients are 0.01 to 1% vitamins, particularly the B complex vitamin, B1, B2, niacin and Vitamin C and 3 to 10% of minerals and trace elements, as a percentage of total mass of extract.

Typically, the macro nutrients are 20-40% lipids, 10-50% proteins and 1 to 25% carbohydrates as a percentage of total mass of extract.

The invention also provides a process for making a pharmacologically and biologically active composition extracted from carrots comprising the steps of

- communuting cleaned and washed carrots to obtain a homogeneous comminution;
- separating the juice from the comminution by filtration;
- treating the juice with a carboxylic acid to adjust the pH of the juice to between 3 and 6;
- treating the pH adjusted juice with at least one saccharide;
- centrifuging the saccharide containing juice to obtain the composition in a paste form.

In accordance with another embodiment of this invention the process includes a further step of drying the paste in vacuum and pulverizing the solid material so formed to obtain the composition in particulate form.

Typically, the carboxylic acid is at least one acid selected from a group consisting of mono carboxylic acid such as, ascorbic acid and/or sorbic acid, and/or a dicarboxylic acid such as adipic acid, malic acid, fumaric acid or tartaric acid or mixtures of them, and/or a tricarboxylic acid such as citric acid, in solid form or as a saturated aqueous solution in an amount of acid equivalent to 0.03-3.0% mass of juice.

Typically, the saccharide is at least one selected from a group consisting of monosaccharide such as fructose and/or dextrose, and/or a disaccharide such as sucrose, lactose, and/or hexitols such as mannitol, sorbitol, either in solid form or as a saturated aqueous solution, in an amount of saccharide ranging from 1-50% of the juice, preferably 20-30% of the mass of juice.

According to this invention there is further provided a method of treating the human or animal body, therapeutically or prophylactically for conditions arising from a retinoid deficiency state, oxidative stress, Wald's cycle aberration, pathological keratinization, malignancies or for immunomodulation, by administering orally in suitable tablet, capsule or liquid dosage form or topically a pharmaceutical or biological composition which contains, extracted from carrots, a 0.25 to 5% mass of active carotenoid fraction

as a percentage of total mass of extract in combination with micro and macro nutrients aiding in the absorption, assimilation and supplementing the action of the carotenoid fraction.

In accordance with one preferred embodiment of this invention the method also provides for including in the administered composition therapeutic amounts of at least one substance selected from a group containing spirulina, Vitamin E, Vitamin C, selenium compounds, zinc compounds, naturally occurring carotenoids such as those found in algae, fruits and vegetables.

In the sub therapeutic form the pharmacologically and biologically active composition extracted from carrots can be used as a biocompatible pigment.

DETAILED DESCRIPTION OF THE INVENTION

A principal object of the present invention is to provide a pharmacologically and biologically active composition extracted from carrots (*Daucus carota L.*), including 0.25-5% mass as a percentage of total mass of extract of active carotenoid fraction, absorbable by an animal or human body in a convenient dosage form, in combination with micro and macro nutrients aiding in the absorption, assimilation and supplementing the action of the carotenoid fraction.

A feature of this invention is that the extracted composition is compatible with the different natural constituents of the composition, namely the individual and total carotenoids, vitamins, proteins, lipids, carbohydrates, minerals and trace elements and other such naturally-occurring constituents as analyzed by methods known in the literature. The amount of different naturally occurring constituents of carrots, is determined to lie within the ranges specified in the description below and in the accompanying examples. Generally for carrots, the ranges per 100 grams of isolated powder is 250-5000 mg total carotenoids, 10-1000 mg vitamins, 10-50 g proteins, 20-40 g lipids, 1-25 g carbohydrates and 3-10 g minerals & trace elements.

A second object of the present invention is to describe a novel process for the preparation of the composition from carrots. As one particular example according to the invention, fresh, hard, good quality, orange or red colored carrots with a smooth surface are selected. Different reddish varieties of carrots such as for example "Pusa Kesar", "Pusa Meghali", "Desi Red" are available. Orange-coloured varieties such as "Bangalore local" and "Ooty Hybrid" are known to be rich in beta-carotene, while the reddish-coloured varieties are more rich in lycopene. The carrots are thus selected for process depending on the nature of the composition to be prepared. Defective carrots are eliminated or excluded in the sorting out process. The selected carrots are washed thoroughly with water and comminuted in an appropriate mill, typically a fruit mill which consists of a rotating stainless steel blades whose speed of rotation is adjustable to between 100 to 1000 rpm and which is fitted with a sieve with apertures variable from 1 to 10 mm to control the particle size of the homogeneous comminution. The comminution is treated through a filter press or a coarse filter (50-150 microns) for the purpose of separating the pulp from the juice. To the juice is added with stirring a mono-carboxylic acid such as ascorbic acid, and/or sorbic acid, and/or a dicarboxylic acid such as adipic acid, malic acid, fumaric acid or tartaric acid or mixtures of them, and/or a tricarboxylic acid such as citric acid, in solid form or as a saturated aqueous solution in an amount of acid equivalent to 0.03-3.0% of the liquid, such that a pH value of the

resulting mixture of about 3.0–6.0, preferably 5.0 is reached. This helps to build up the particle size of colloidal carotenoid complexes enabling the further processing of the juice by filtration or centrifuging. The carboxylic acids also stabilise the juice during processing. To the resulting solution or suspension is added one or more components of a monosaccharide such as fructose and/or dextrose, and/or a disaccharide such as sucrose, lactose, and/or hexitols such as mannitol, sorbitol, either in solid form or as saturated aqueous solution, in an amount of saccharide ranging from 1–50% of the juice, in particular 20–30% of the carrot juice, which mixture is subjected to centrifugation to provide carotenoids-rich carrot paste containing 0.1–1.0% carotenoids. It has been observed that the use of saccharides not only increases the stability of the carotenoid fraction but also is instrumental in extracting the carotenoid fraction bound to lipoproteins in combination with micronutrients such as the B-complex vitamins and minerals. In the absence of the saccharides step, the concentration of micro nutrients in the final composition is less than 50 per cent. Moreover, in the absence of the above, the carotenoids degrade within a few months storage. The carotenoids-rich paste can be used as such or after drying under high vacuum, pulverizing and sieving through appropriately sized sieves by which the pharmacologically and biologically active composition of the invention is obtained in powder form.

The powder is analyzed according to known procedures to provide the precise composition of the carotenoids, vitamins, minerals & trace elements, proteins, carbohydrates and lipids in the powder.

The present invention also describes the use of the paste or powder of the invention in health care and nutrition applications and as a colouring agent. The paste can be formulated as an emulsion or suspension for oral or topical use or as a colouring matter using appropriate excipients and adjuvants known to those skilled in the formulations art. The powder can be formulated as solid dosage forms for oral use as powder/granules or as capsules/tablets. These can also be combined with other antioxidants, minerals, vitamins and other micronutrients. Carotenoids act as lipid phase antioxidants. However beta-carotene supplementation alone does not appear to reduce the susceptibility of LDL to oxidation. The present invention also discloses a method of treating the human or animal body, therapeutically or prophylactically for conditions arising from a retinoid deficiency state, oxidative stress, Wald's cycle aberration, pathological keratinization, malignancies or for immunomodulation, LDL cholesterol reduction, cancer adjuvant therapy and reducing risk of cardiovascular disease by administering orally in suitable tablet, capsule or liquid dosage form or topically a pharmaceutical or biological composition which contain extracted form carrots, a 0.25 to 5% mass of active carotenoid fraction as a percentage of total mass of extract in combination with micro and macro nutrients aiding in the absorption and assimilation and supplementing the action of the carotenoid fraction. Inflammatory and allergic manifestations in the living cell are thought to be the direct cause of hyperactivity of immune function entities in non-specific immunity, whereas the suppression or deficiency of immune functions are the result of hypoactivity. The functioning and efficiency of non-specific immunity may be influenced by many exogenous and endogenous factors like physical and psychological, oxidant or hyperoxidative stress, hormonal imbalance, pharmaceuticals and the like. A recent trend in medicine is to consider all disease from the molecular perspective, in which derangements in the structures or conformations of vital biomolecules in diseased states are

intricately implicated in the aetiopathogenesis of those diseased conditions.

'Immunomodulation' is any procedure which can alter non specific immunity by interfering with its functioning. If it results in enhancement of immune reactions, it results in immunostimulation and primarily implies stimulation of the non specific immunity, that is stimulation of the function and efficiency of granulocytes, macrophages, natural killer cells, complement and properdin, and the various effector substances including interleukins, tumour necrosis factor, interferons, lysozymes, prostaglandins, oxygen radicals and other mediators. Immunosuppression mainly implies reduced resistance against infections and stress and may be due to environmental or chemotherapeutic factors.

15 Immunostimulation and immunosuppression both need to be addressed in order to regulate normal immunological functioning. Hence, immunostimulating and immunosuppressing agents both have their own standing. There are a variety of known immunosuppressing agents, for instance cyclosporin, however few immunostimulating agents are available. Apart from specific stimulative or suppressive activity, it is believed that certain agents of plant origin such as the carotenoids have the activity to normalize or modulate pathophysiological processes in the underlying immune response and hence the term immunomodulation or immunomodulatory agents or adaptogenic agents are used for these agents. This activity is believed to be dose dependant as can be seen from the immunostimulation at low dilutions of many immunosuppressants. Thus in a biological system, 20 active material will act as an immunostimulant in low doses but as an immunosuppressant in high doses. Such a biologically active material can be called as an 'immunomodulator'.

25

Biological membranes contain phospholipids (PLs) and degradation of these by oxygen can cause loss of cell integrity. PLs contain high quantities of polyunsaturated fatty acids (PUFAs) and the double bonds of these fatty acids are easily attacked by oxygen to produce toxic fatty peroxides. The extent of formation of peroxides (peroxidation) increases with the number of double bonds in the fatty acids of the PLs, so membranes with a high PUFA content are specially likely to be more oxidized. A common example of peroxidation is rancidity of butter and vegetable oils. Another agent produced within and without the cell is called 30 a free radical. These substances are highly reactive because they are chemically incomplete and hence unstable, so they can latch on to other substances very readily. They are also known as super oxide radicals (singlet oxygen) and they are produced within the cells both by self-oxidation (as in peroxides) and by enzymatic processes. Their high intrinsic reactivity and their ability to generate even more potent oxidizing agents when combined with peroxides constitutes a constant threat to cellular integrity. It must be admitted that free radicals perform some useful functions: the bactericidal 35 action of leucocytes and in mediating inflammatory responses are notable examples, but it is when they are produced in large quantities and their metabolic products are allowed to go unchecked that they can seriously damage membranes and even denature DNA. Increased generation of free radicals in the biological systems over and above the potential of antioxidant mechanisms to curb them produces a state what is commonly known as oxidative (oxidant) stress in the body. Since free radicals are continuously being generated, the human body has developed a number of mechanisms to deal with their potentially damaging effects and those of their metabolites. The susceptibility of any tissue to an oxidative stress induced by free radicals or

40

45

50

55

60

65

peroxide relates to the balance between the extent of that stress and the antioxidant ability of the protective agents present. 'Health' can be defined as an equilibrium state between the generation and scavenging of free radicals and peroxides. The cellular defense mechanisms and scavenging agents involve various enzymes such as superoxide dismutase, glutathione synthetase, glutathione peroxidase, glutathione reductase, glucose-6-phosphate, dehydrogenase and catalase. Plasma proteins with antioxidant potential include the copper containing transferrin, ceruloplasmin and the iron containing transferrin. Foods constituents that also contribute to protection include the sulphur containing amino-acids and the minerals selenium, zinc and copper. In most pathological conditions the protective antioxidant mechanisms are overwhelmed leading to an elevated or rising state of free radicals and peroxides. Both Vitamin E and carotenoids can successfully deactivate super oxides (singlet oxygen) but when Vitamin E attacks the oxide it is destroyed. On the other hand beta-carotene can quench the oxide without damage to itself and thus can be used again and again and can convert singlet oxygen back to normal oxygen before it can cause damage leading to skin or lung cancer. Beta-carotene is also very efficient at trapping the free radicals.

Hence the present invention also encompasses that in the process of the preparation of formulations, there may be added adjuvants to the composition of the invention, such adjuvants being Vitamin C, Vitamin E, Compounds of selenium such as Selenium Dioxide and compounds of zinc such as Zinc Sulphate and additional amounts of commercially available natural-sourced carotenoids such as from fruits, vegetables and algae. The composition of typical preparations are described under respective examples.

The formulations of the invention are useful for the prophylactic or therapeutic treatment of subjects diagnosed to be carotenoid-deficient or Vitamin A-deficient or in need of protective efficacy of antioxidants known to be implicated in chronic disorders such as heart diseases, cancer, cataract and other chronic ailments. Both human and veterinary use is envisaged. The dosage per day is variable dependent on the age and weight of the subject to be treated and the severity of the condition as assessed by practicing medical physicians.

The following examples illustrate but do not limit the scope of the invention.

EXAMPLE 1

Fresh, hard, good quality reddish colored "Desi Red" carrots with a smooth surface, excluding those that were found defective, were selected and washed thoroughly with water. The sorted and washed carrots (1.0 kg) were subjected to crushing in a fruit mill to provide a comminution which was subjected to pressing through a filter press for the purpose of separating the pulp from the juice to provide a juice (ca. 600 ml). To the juice, 3 g of adipic acid was added with stirring. To the resulting mixture was added 60 g of sorbitol and the mixture was subjected to centrifuging to provide paste (ca. 17.2 g). The paste was dried under high vacuum. Pulverizing of the solid material and sieving gave the carotenoid powder of the invention (3.8 g). The composition of the product is given below.

Composition per 100 g Product from "Desi Red" Carrots (Example 1)

5	beta-Carotene	530 mg
	alpha-Carotene	27 mg
	Lycopene	700 mg
	Lutein/Xeaxanthin	15 mg
10	Total Carotenoids	3750 mg
	Proteins	32.8 g
	Carbohydrates	4 g
	Phosphorus	647 mg
	Lipids	15.3 g
	Vitamin C	22 mg
	Vitamin B1	5 mg
	Vitamin B2	1 mg
	Iron	95 mg
	Zinc	1 mg
	Manganese	1 mg
	Magnesium	162 mg
	Calcium	1.381 g
	Potassium	1.99 g
	Sodium	1.99 g
	Total Minerals (Ash value)	6.87 g

EXAMPLE 2

The "Bangalore local" carrots were processed according to the procedure described in Example 1. The composition of the product is given below.

Composition per 100 g Product from "Bangalore local" Carrots

35	beta-Carotene	2095 mg
	alpha-Carotene	31 mg
	Lycopene	70 mg
	Lutein/Xeaxanthin	13 mg
40	Total Carotenoids	2948 mg
	Phosphorus	680 mg
	Proteins	31.5 g
	Carbohydrates	4.5 g
	Lipids	30.3 g
	Vitamin C	24 mg
	Vitamin B1	6 mg
	Vitamin B2	2 mg
	Iron	12 mg
	Zinc	1.4 mg
	Manganese	1 mg
	Magnesium	602 mg
	Calcium	894 mg
	Potassium	2 g
	Sodium	1 g
	Total Minerals (Ash value)	7.1 g

EXAMPLE 3

The different supplies carrots were processed according to the procedures described in Examples 1 to 13. The composition of the powder was analyzed and shown to have values in the range as described below.

Range of composition per 100 g products from carrots (*Daucus carota L.*)

60	beta-Carotene	100-4000	mg
	alpha-Carotene	10-300	mg
	Lycopene	10-2000	mg
	Lutein/Xeaxanthin	5-50	mg
	Total Carotenoids	250-5000	mg

-continued

Proteins	10-50	g
Carbohydrates	1-25	g
Phosphorus	0.1-1	g
Lipids	20-40	g
Vitamin C	10-500	mg
Vitamin B1	1-6	mg
Vitamin B2	0.5-4	mg
Iron	5-100	mg
Zinc	1-5	mg
Manganese	0.1-1	mg
Magnesium	50-900	mg
Calcium	0.5-3	g
Potassium	1-4	g
Sodium	1-3	g
Total Minerals (Ash value)	3-10	g

Typical composition of Ingredients:

5	Nutrient-rich carotenoid powder (cf Example 1)	400 mg
	Gelatin	12 mg
	Sucrose	25 mg
	Microcrystalline Cellulose	25 mg
	Starch	60 mg
	Talc	5 mg
	Magnesium stearate	3 mg
10	Colloidal Silicon dioxide	10 mg
	Hydroxy Propyl Methyl Cellulose	15 mg
	Titanium Dioxide	0.5 mg
	Sunset Yellow FCF	4 mg
	Propylene Glycol	1 mg

15

The tablets were prepared by blending nutrient-rich carotenoid powder with sucrose and Microcrystalline cellulose, granulating with Starch Gelatin paste, drying, lubricating with Talc, Magnesium stearate and Colloidal silicon dioxide followed by compression into tablets. For coating, Hydroxypropyl Methyl Cellulose, Propylene glycol and a blend of Titanium dioxide/Sunset Yellow FCF were used.

EXAMPLE 4

The procedure described in Example 1 was followed 20 using citric acid in place of adipic acid.

EXAMPLE 5

The procedure described in Example 1 was followed 25 using fumaric acid in place of adipic acid.

EXAMPLE 6

The procedure described in Example 1 was followed 30 using malic acid in place of adipic acid.

EXAMPLE 7

The procedure described in Example 1 was followed 35 using tartaric acid in place of adipic acid.

EXAMPLE 8

The procedure described in Example 1 was followed 40 using ascorbic acid in place of adipic acid.

EXAMPLE 9

The procedure described in Example 1 was followed 45 using sorbic acid in place of adipic acid.

EXAMPLE 10

The procedure described in Example 1 was followed 50 using mannitol in place of sorbitol.

EXAMPLE 11

The procedure described in Example 1 was followed 55 using sucrose in place of sorbitol.

EXAMPLE 12

The procedure described in Example 1 was followed 60 using lactose in place of sorbitol.

EXAMPLE 13

The procedure described in Example 1 was followed 65 using dextrose in place of sorbitol.

EXAMPLE 14

Preparation of nutrient-rich carotenoids tablets.

EXAMPLE 15

Preparation of nutrient-rich carotenoid in combination 20 with other antioxidants in tablet form.
Typical composition of ingredients:

30	Nutrient-rich carotenoid powder (cf Example 1)	100 mg
	Natural beta-carotene and carotenoids 20%	15 mg
	Vitamin E Acetate	25 mg
	Vitamin C	150 mg
35	Selenium dioxide	75 mcg
	Zinc, sulphate	70 mg
	Microcrystalline Cellulose	25 mg
	Starch	25 mg
	Gelatine	5 mg
	Talc	6 mg
40	Magnesium Stearate	4 mg
	Colloidal Silicon Dioxide	6 mg
	Hydroxypropyl Methyl Cellulose	15 mg
	Titanium Dioxide and Sunset Yellow FCF	0.5 mg
	Propylene Glycol	1 mg

Tablets were prepared by blending nutrient-rich carotenoid powder with Vitamin E acetate, Vitamin C, Selenium Dioxide and Zinc Sulphate. The blend was mixed with Microcrystalline Cellulose, granulated with Starch paste, dried, lubricated with Talc, Magnesium stearate and Colloidal Silicon Dioxide followed by compression into tablets. For coating, Hydroxypropyl Methyl Cellulose, Propylene glycol Titanium Dioxide and Sunset yellow FCF were used.

EXAMPLE 16

Preparation of tablets of nutrient-rich carotenoid with spirulina: typical composition of ingredients

55	Nutrient-rich carotenoid Powder (ef example 1)	250 mg
	Spirulina	250 mg
	Microcrystalline Cellulose	50 mg
	Starch	15 mg
	Talc	6 mg
	Magnesium Stearate	4 mg
60	Colloidal Silicon Dioxide	6 mg

65 The tablets were prepared by blending nutrient-rich carotenoid powder, Spirulina and Microcrystalline Cellulose, granulated with starch paste, dried, lubricated with Talc,

11

Magnesium Stearate and Colloidal Silicon Dioxide and
compressed into tablets.

EXAMPLE 17

Preparation of nutrient-rich carotenoid capsules
Typical composition of ingredients

Nutrient-rich carotenoid powder (cf example 1)	250 mg
Microcrystalline Cellulose	100 mg
Talc	7 mg
Magnesium Stearate	2 mg
Colloidal Silicon Dioxide	4 mg

Nutrient-rich carotenoid powder was blended with Micro-crystalline Cellulose, lubricated with Talc, Magnesium Stearate, Colloidal silicon dioxide and filled in the capsules.

EXAMPLE 18

Preparation of nutrient-rich carotenoid Soft Gelatin Capsules
Typical composition of ingredients

Nutrient-rich carotenoid powder (cf example 1)	250 mg
Vegetable oil	250 mg
Soft gelatin capsule shell	one

EXAMPLE 19

Preparation of nutrient-rich carotenoid powder mix
Typical composition of ingredients

Nutrient-rich carotenoid powder (cf example 1)	500 mg
Sucrose	500 mg

Nutrient-rich carotenoid powder was blended with sucrose and filled in 40 micron Aluminium-poly sachets.

EXAMPLE 20

Preparation of suspension of micronutrient-rich carotenoid paste
Typical composition of ingredients

Nutrient-rich carotenoid paste (cf Example 1)	20 g
Sucrose	60 g
Purified water to make	100 ml

Nutrient-rich carotenoid paste was suspended in syrup prepared from sucrose and water.

EXAMPLE 21

Preparation of cream containing nutrient-rich carotenoid paste
Typical composition of ingredients

Nutrient-rich carotenoid paste (cf Example 1)	1 g
Vitamin E Acetate	1 g

12

-continued

Vitamin C	1 g
Light Liquid Paraffin	10 g
Propylene Glycol	8 g
Cetostearyl alcohol	7 g
Cetomacrogol - 1000	3.5 g
White Bees Wax	2.5 g
Purified Water	66 g

A blend of nutrient-rich carotenoid paste, Vitamin E acetate and Vitamin C was incorporated in cream prepared from solution of Cetostearyl alcohol, Cetomacrogol 1000 and White beeswax in light liquid paraffin and water-propylene glycol mixture.

Tablets(Example 14) containing 400 mg of the composition equivalent to 1.2 mg of carotenoid were used for trials:

GROUP I

5 participants complaining of watering of eyes, redness and inability to open the eyes completely in sunlight were administered the tablets over a period of two weeks. Significant reduction of the symptoms were observed.

GROUP II

5 participants sensitive to continuous exposure to sunlight and suffering from skin erythema on longer exposure were administered the tablets over a period of four weeks. Significant reduction of the symptoms induced by long exposure were observed.

We claim:

1. A method of inducing antioxidant activity in warm-blooded animals comprising administering to warm-blooded animals an antioxidantly effective amount of a biologically active composition comprising 0.25 to 5% by weight of an active carotenoid fraction extracted from carrots with a carboxylic acid at a pH of 3 to 6 followed by treatment with at least one saccharide based on the total weight of the composition and micro and macro nutrients sufficient to aid in the absorption acid assimilation of the carotenoid fraction and to supplement the action thereof.

2. The method of claim 1 wherein the composition also contains therapeutic amounts of at least one member of the group consisting of spirulina, Vitamin E, selenium compounds, zinc compounds, Vitamin C and carotenoids extracted from other natural sources.

3. The method of claim 1 wherein the macro nutrients include 20 to 40% by weight of the composition of lipids.

4. The method of claim 1 wherein the macro nutrients include 10 to 50% by weight of the total composition of proteins.

5. The method of claim 1 wherein the macro nutrients include 1 to 25% by weight of the total composition of carbohydrates.

6. The method of claim 1 wherein the micro nutrients include 0.01 to 1% by weight of the total composition of at least one vitamin selected from the group consisting of Vitamins B₁ and B₃, Niacin and Vitamin C.

7. The method of claim 1 wherein the micro nutrients include 3 to 10% by weight of the total composition of materials and trace elements.

8. The method of claim 1 wherein the carotenoid fraction includes α-carotene, β-carotene, Lutein, zeaxanthin and lycopene.

* * * * *